locities of certain ketones with the above reagents have been made. The results suggest that steric hindrance of the carbonyl group is responsible for wide variations in the rate of reaction.

3. It has been shown that the addition of pyridine displaces the oxime synthesis equilibrium in the direction of completion.

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[CONTRIBUTION FROM THE AMMONIA DEPARTMENT OF E. I. DU PONT DE NEMOURS AND COMPANY]

Rapid Determination of Hydroxyl by Means of Acetyl Chloride and Pyridine

BY DONALD MILTON SMITH AND W. M. D. BRYANT

The most widely used quantitative procedures for determining the hydroxyl radical in organic compounds are probably those based on the use of acetic anhydride with or without the addition of pyridine.[1,2,3,4] When carried out in the approved manner, these methods though precise are time-consuming, due either to the slow rate of reaction or the elaborate precautions necessary in analyzing volatile materials.

Although the use of acetyl chloride as a qualitative reagent for alcohols and certain amines is described in most laboratory texts, less information is available regarding the quantitative value of this substance. One textbook, that of Thorpe and Whiteley,[5] recommends the use of acetyl chloride in the identification of alcohols. The authors claim quantitative yields of ester in one case, but their procedure is apparently preparative rather than analytical in character.

In the present research advantage was taken of the high rate of reaction of acetyl chloride with hydroxyl compounds, and a quantitative titrimetric method of exceptionally wide scope developed. The method is rapid, requires only simple apparatus and yields results which compare favorably with the less rapid acetic anhydride methods.

The new acetyl chloride procedure is applicable to monohydroxy primary and secondary alcohols, both aliphatic and aromatic, to phenols, and to such polyhydroxy compounds as are appreciably soluble in the reagent. Primary and secondary hydroxyl groups present with other functional groups in such molecules as hydroxyglycerides react quantitatively. Tertiary alcohols do not in general react quantitatively. The active hydrogen in mercaptans and primary and secondary amines could probably be estimated by this method, although no experiments with these classes of compounds were included in the present program.

In principle the procedure is similar to the acetic anhydride–pyridine method of Verley and Bölsing,[2] but offers certain advantages not found in their method. Under similar conditions of concentration and temperature, acetyl chloride is considerably more reactive than acetic anhydride. The more recent modifications of the acetic anhydride–pyridine procedure require more time for the reaction to go to completion.[1,3,4] Also, the interference of aldehydes is less pronounced where acetyl chloride is employed.

Comparative experiments indicate that the absolute accuracy is as good as that of the acetic anhydride–pyridine method. The average precision of the acetyl chloride method, however, is slightly less (±0.5% compared with ±0.2% for the older method).

Experimental

Reagents.—The acetylating reagent was prepared by mixing 1.5 moles (approx. 118 cc.) of Eastman Kodak acetyl chloride (No. P-334) with dry J. T. Baker's C. P. toluene sufficient to make 1 liter of solution. Dry Baker's C. P. pyridine was used in conjunction with the above reagent.

Compounds Investigated.—A few alcohols and all of the phenols were obtained from the Eastman Kodak Co. and used without further purification. The remaining alcohols used were obtained from various sources and carefully purified by fractional distillation. The boiling ranges of the purified compounds are included in Table I. The fractionated alcohols were mostly of 99% purity or better. 2-Methylbutanol-1, hexanol-1 and 2-ethylbutanol-1 could not be freed completely of contaminants by distillation but were probably at least 97% pure.

Analytical Procedure.—Ten cc. of 1.5 molal acetyl chloride in toluene is pipetted into a dry 250 cc. g. s. volumetric flask (calibration unnecessary) using a Lowy auto-

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[1] W. Normann and E. Schildknecht, *Fettchem. Umschau*, **40**, 194 (1933).

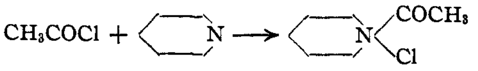
[2] A. Verley and Fr. Bölsing, *Ber.*, **34**, 3354 (1901).

[3] V. L. Peterson and E. S. West, *J. Biol. Chem.*, **74**, 379 (1927).

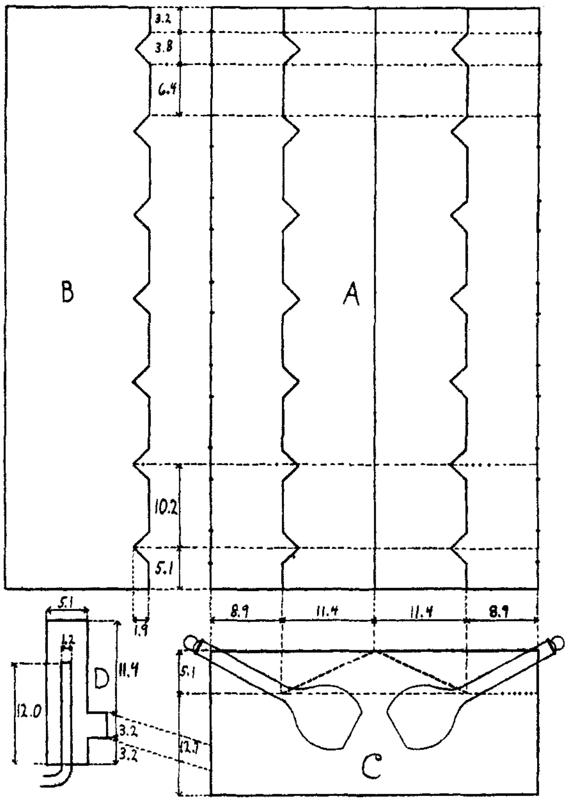
[4] S. Marks and R. S. Morrell, *Analyst*, **56**, 428 (1931).

[5] J. F. Thorpe and M. A. Whiteley, "A Students' Manual of Organic Chemical Analysis," Longmans, Green & Co., Ltd., London, 1926.

matic pipet. The flask is then placed in a beaker containing a slurry of finely chopped ice and after standing a minute or so, 2 cc. of pyridine is added from a pipet. The mixture is then stoppered and shaken. A thin paste of acetyl pyridinium chloride in toluene results



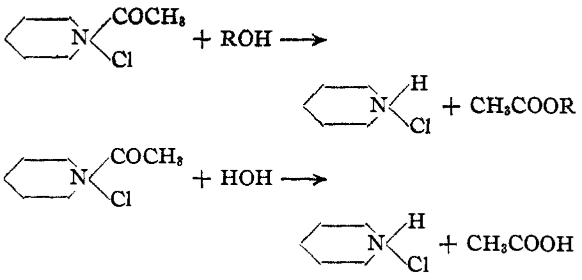
A known weight or volume of dry sample is added in such proportions that an excess of 0.5 mole of acetyl chloride is always present for each mole reacted. Where the sample is a solid, 5 cc. of toluene is added to wash down adhering particles from the neck of the flask. The flask is shaken and placed in a water-bath (Fig. 1) at 60 ± 1°, loosening the stopper momentarily to expel air. The flask is then stoppered firmly, heated for twenty minutes with occasional shaking, then removed from the bath and cooled in ice water; 25 cc. of distilled water is added to decompose the unused reagent. It is necessary to shake the mixture vigorously to complete the decomposition in the toluene layer before adding indicator.



Dimensions in centimeters.

Fig. 1.—Construction of water-bath: A, top view of bath; B, side; C, end view showing position of flasks; D, constant level of overflow.

The mixture is titrated directly to a phenolphthalein end-point. At least one blank determination should be run with each group of samples. The decrease in acidity of the sample over that of the blank is a direct measure of the alcoholic hydroxyl present in the sample. The results are calculated on the basis of the two following reactions



Both acetic acid (or pyridine acetate) and pyridine hydrochloride can be titrated using phenolphthalein as the indicator.

The samples should be dry or contain at most only a few per cent. of water. As is obvious from the above equation, water decomposes and thus renders unavailable a part of the reagent. Because of its low molecular weight, a small amount of water can decompose a considerable amount of reagent.

Since the reagent contains a volatile substance (CH_3COCl), a uniform dispensing technique was developed to minimize losses during handling, particularly those of an irregular character not covered by the blank. The acetyl chloride reagent is quite stable when kept in glass stoppered bottles. Minor variations arising from volatilization or temperature changes are taken care of by the blank.

The water-bath shown in Fig. 1 is very convenient where several samples are to be analyzed at one time. It consists of a rectangular copper pan with principal dimensions of 71.1 × 40.6 × 17.8 cm. A strip of copper sheet 71.1 cm. long and 25.4 cm. wide bent at an angle of 130° parallel to the long dimension is soldered to the end faces of the bath as illustrated. The long edges of the bath and the center strip are cut with a series of V-shaped notches 1.9 cm. deep and 3.8 cm. wide, spaced at regular intervals. When the bath is filled with water to a depth of 12.0 cm., volumetric flasks (250 cc. size) are held firmly in the notches by buoyancy and require no other means of support. The depth of water is maintained by means of a constant level overflow. An iron stand supports the bath at a convenient height. A bath of the size specified can easily be held at 60 ± 1° by a single Fisher burner without any thermostatic arrangement.

Analytical Results

The experimental results obtained with a large number of alcohols and phenols are given in Table I. The majority of the results differ from the theoretical by less than 2%. The data for phenols showed less satisfactory apparent agreement. However, in this case the trade products were used without further purification, a fact which may explain the low results obtained.

Benzoin reacted only to the extent of 93%. This was probably a result of incomplete reaction or low solubility in the reaction environment. Incomplete reaction was obtained in the case of anhydrous glucose (Eastman chemical) due to unsatisfactory solubility relations. Slight modi-

TABLE I

ANALYTICAL DATA FOR ALCOHOLS AND PHENOLS

Substance	Boiling range obsd., °C.	Detns.	% of theoretical hydroxyl content	Method of sampling
Ethanol	78.3	3	99.1 ± 0.2	Gravimetric
n-Propanol[a]	97.2– 97.3	3	98.8 ± 0.3	Gravimetric
Isobutanol	107.5–107.8	20	98.9 ± 0.2	Gravimetric
n-Butanol	116.6–116.8	5	98.7 ± 0.2	Gravimetric
Pentanol-3	116	2	98.9 ± 0.4	Gravimetric
2-Methylbutanol-1	128–129	2	97.2 ± 0.2	Gravimetric
Hexanol-1	156.0–157.4	3	96.6 ± 0.1	Calib., volumetric
2-Methylpentanol-1	148–149	9	98.1 ± 0.5	Gravimetric
2-Methylpentanol-4	131.3–131.8	6	99.1 ± 0.2	Gravimetric
2-Ethylbutanol-1	148.0–148.2	6	96.8 ± 0.5	Gravimetric
2,4-Dimethylpentanol-1	157–159	3	98.9 ± 0.5	Gravimetric
2,4-Dimethylpentanol-3	138–139	3	99.1 ± 0.1	Gravimetric
Octanol-1	195.1–195.3	3	100.2 ± 0.7	Gravimetric
Octanol-2	175–177	4	97.8 ± 0.2	Calib., volumetric
2-Ethylhexanol-1	184.1	3	98.8 ± 0.4	Gravimetric
2,4-Dimethylhexanol-3	157–159	3	100.7 ± 0.5	Gravimetric
Decanol-1	230.0–230.7	3	98.6 ± 0.3	Gravimetric
Dodecanol-1	263.2–264.4	3	98.5 ± 0.2	Gravimetric
Tetradecanol-1	295.0–295.8	3	98.3 ± 0.4	Gravimetric
Glycerol[b]	....	3	95.4 ± 0.3	Gravimetric
Cyclohexanol	159.0–160.5	3	101.1 ± 0.4	Calib., volumetric
Borneol[c]	....	3	98.4 ± 0.2	Gravimetric
Benzyl alcohol	87 (8 mm.)	3	99.0 ± 0.3	Gravimetric
Cinnamyl alcohol[c]	....	2	97.9 ± 0.1	Gravimetric
Benzoin[c]	....	3	93.3 ± 0.6	Gravimetric
Phenol[d]	....	1	95.8	Volumetric, uncalibrated
Quinol[c]	....	2	93.1 ± 1.4	Gravimetric
Pyrogallol[c]	....	2	95.2 ± 0.8	Gravimetric
o-Cresol[d]	....	1	93.1	Volumetric, uncalibrated
m-Cresol[d]	....	3	95.0 ± 0.5	Gravimetric
p-Cresol[d]	....	1	94.6	Volumetric, uncalibrated
Guaiacol[c]	....	1	97.0	Volumetric, uncalibrated
Xylenol[c] (CH_3, CH_3, OH = 1, 3, 4)	....	1	92.5	Volumetric, uncalibrated
α-Naphthol[c]	....	2	97.9 ± 0.1	Gravimetric
Thymol[c]	....	3	94.2 ± 0.8	Gravimetric

[a] Results corrected for 0.4% ketone. [b] Baker's analyzed, c. p. grade. [c] Eastman chemicals. [d] Eastman practical chemicals.

fication of the method would probably rectify this difficulty since both benzoin and glucose have been analyzed successfully by the acetic anhydride method.[3] Contrary to the experience of Verley and Bölsing,[2] no difficulty was encountered in the case of benzyl alcohol.

Tertiary alcohols (exclusive of phenols) apparently do not react completely with acetyl chloride and pyridine. Experiments with Eastman *t*-butanol and 2-methylpentanol-2 gave results indicative of only 30 to 40% reaction. This tendency is even more marked where the acetic anhydride–pyridine procedure is used. Experiments in which the samples were heated for twenty minutes at 60° with 10 cc. of a 1.5 molal solution of acetic anhydride in pyridine showed only 1.5% reaction with *t*-butanol. The three earlier references cited above make no specific mention of the fact that tertiary alcohols are unreactive. It is interesting to note, however, that terpineol and linalool, the only tertiary alcohols investigated by Verley and Bölsing, both gave very low results.

Comparative Reactivity of Acetyl Chloride and Acetic Anhydride with Alcohols in the Presence of Pyridine

A group of experiments designed to show the comparative rates of reaction of acetyl chloride and acetic anhydride with typical primary and secondary alcohols indicated that acetyl chloride is much more reactive. For the acetyl chloride experiments the regular reagents were employed in their usual proportions. The 1.5 molal acetic anhydride in pyridine described above was used for the others. Isobutanol and 2,4-dimethylpentanol-3 were selected as typical alcohols. The results are given in Table II.

Table II

Relative Reactivity of Acetyl Chloride and Acetic Anhydride in the Presence of Pyridine

Experimental conditions		% of theoretical hydroxyl content			
		Isobutanol		2,4-Dimethylpentanol-3	
Time, min.	Temp., °C.	AcCl-Py	Ac_2O-Py	AcCl-Py	Ac_2O-Py
15	Cold	98.7	48.4	53.9	2.7
20	60	98.9	85.6	99.1	23.9
40	60	..	94.3	..	36.3

The above modification of the acetic anhydride procedure is not the most advantageous one for analytical use. Its application was restricted to the problem of comparative reaction rates.

Comparative Precision and Accuracy of Acetyl Chloride and Acetic Anhydride Methods

The acetic anhydride procedure found most satisfactory from the standpoint of precision and accuracy is essentially that of Marks and Morrell. The reaction flasks, however, were connected with reflux condensers by means of ground glass joints and were heated in boiling water (100°) for two hours.

Careful comparative experiments were made using a number of pure alcohols with both the above procedure and the recommended acetyl chloride procedure. These are recorded in Table III. The letters A, B and C are employed to differentiate the work of three different analysts. The numerical data included in Table III are the analyses of exceptionally pure alcohols. These data serve to illustrate not only the agreement between the two methods, but also the absolute accuracy and experimental precision attainable in each, as well as the extent to which the personal equation may be expected to affect the results.

Marks and Morrell found that the hydroxyl groups of ricinolein in castor oil were readily estimated by the acetic anhydride–pyridine procedure. It consequently seemed desirable to try some comparative experiments by both methods using this material. The following results were obtained with a sample of "crystal" grade product obtained from the Baker Castor Oil Co.:

Method	Experiments	% of triricinolein
AcCl-Py	3	94.1 ± 0.3
Ac_2O-Py	3	93.7 ± 0.4

The agreement between the two methods is again entirely satisfactory. Castor oil is not composed exclusively of ricinoleic glyceride, hence the slightly low results.

Interfering Substances.—The acetyl chloride and acetic anhydride procedures are both affected by the presence of certain other compounds in the sample for analysis. Primary and secondary amines, mercaptans and the higher fatty acids react to a varying extent with the above reagents to form stable products which would be analyzed as esters. Formic esters of low molecular weight and other products which are readily hydrolyzed by water into an acidic or basic constituent also introduce errors.

Most aldehydes, particularly those of low molecular weight when present in large quantities, have an unfavorable effect upon the end-point in the acetyl chloride procedure. The effect is characterized by a rapid fading of the indicator after the end-point has been attained. If the fading is not too rapid, the latter part of the titration may be carried out by adding alkali in small constant amounts until an end-point perma-

Table III

Analyses of Typical Pure Alcohols

Figures in parentheses indicate number of determinations

	AcCl–Py method		Ac_2O–Py method	
Alcohol[a]	Analyst (A)	Analyst (B)	Analyst (B)	Analyst (C)
Ethanol	(3) 99.1 ± 0.2			
Isobutanol	(12) 98.9 ± 0.3	(8) 98.9 ± 0.1	(3) 98.6 ± 0.2	(6) 98.3 ± 0.4
n-Butanol	(5) 98.7 ± 0.2			
Pentanol-3	(2) 98.9 ± 0.4			
2-Methylpentanol-4	(6) 99.1 ± 0.2			
2-Methylpentanol-1	(9) 98.1 ± 0.5	(3) 98.5 ± 0.3	(3) 98.5 ± 0.1	
2,4-Dimethylpentanol-3	(3) 99.1 ± 0.1	(3) 99.5 ± 0.4	(3) 98.1 ± 0.4	
2-Ethylhexanol-1	(3) 98.8 ± 0.4	(3) 99.6 ± 0.2	(3) 99.7 ± 0.1	
Dodecanol-1[b]	(3) 99.0 ± 0.1	(4) 100.2 ± 0.2	(3) 99.6 ± 0.2	
Benzyl alcohol	(3) 99.0 ± 0.3			

[a] Except where noted, samples are same as those in Table I. [b] B. p. 193° at 100 mm.

nent for thirty seconds is obtained. In addition to the poor end-point, a small amount of reagent is used up by the aldehyde. As much as 10% of aldehyde does not seriously affect the analysis of alcohols. 50% solutions of isobutyraldehyde and 2-methylpenten-2-al-1 both gave unsatisfactory results even when the above precautions were taken. Nevertheless, the acetyl chloride procedure is definitely superior to the acetic anhydride procedure for the analysis of samples containing aldehydes. The latter reagent seems to combine with aldehydes to an appreciable extent and so lead to erroneous hydroxyl determinations.

Ketones produce only slight effects which are readily corrected by control experiments. Analyses of pure samples of acetone, 2-methylpentanone-4 and 2,4-dimethylpentanone-3 showed 1.4, 1.1 and 0.1% reaction calculated as the isomeric unsaturated alcohols.

The authors extend their thanks to Mr. W. A. Morgan for part of the analytical work connected with this research and to Mr. J. B. Evans for analyses of isobutanol and castor oil.

Summary

1. A rapid and precise method for the determination of primary and secondary hydroxyl groups in organic compounds, based on the use of acetyl chloride and pyridine, has been developed. Analytical results for more than thirty alcoholic and phenolic substances are reported.

2. Comparative experiments employing the new method and an accepted form of the acetic anhydride–pyridine method show that the results of the two methods are entirely comparable.

3. Under similar conditions of reagent concentration and temperature and in the presence of pyridine, acetyl chloride is a more reactive acetylating agent than acetic anhydride.

4. The matter of interfering substances is discussed briefly.

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[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Heats of Organic Reactions. I. The Apparatus and the Heat of Hydrogenation of Ethylene

BY G. B. KISTIAKOWSKY, H. ROMEYN, JR., J. R. RUHOFF, HILTON A. SMITH AND W. E. VAUGHAN

The majority of those who have met with the necessity of computing the heat of some organic reaction have probably felt discouraged because of the unreliability of the result obtained, due to uncertainty in the combustion data. Often not even the sign of the heat change, much less its magnitude, can be predicted for small structural change in the molecule. Although the newer work, particularly that of Rossini, greatly exceeds in precision the classical measurements of Thomsen and Berthelot, it is an inherent feature of the method that, as the molecular weight of the substance studied increases, the absolute error in the molar heat of combustion becomes proportionately larger. For this reason, Dr. J. B. Conant and one of the present writers—in common with many others, undoubtedly—have felt the need for a calorimetric procedure capable of yielding more accurate thermal data for higher molecular weight compounds. The direct measurement of the heat of an organic reaction rather than the determination of the difference of the heats of combustion of the reactants and products offers many possibilities. Although this method has been used occasionally in the past, it has never been developed systematically—probably for the reason that not many reactions have been sufficiently quantitative and clean-cut for calorimetric work. However, with catalysts and methods known today, a sufficient number of compounds and reactions can be investigated to make this method worthy of a thorough test.

Catalytic hydrogenations, in particular, seem likely to give interesting and valuable data. Not only can the heat of hydrogenation itself be determined, but by a combination of several such measurements, thermal data for other reactions can be obtained indirectly. The advantage of this device, quite analogous to the combustion method, of course, is that since the heat of hydrogenation is a much smaller quantity than the heat of combustion, more accurate values for the differences in heat content of organic compounds can be obtained, although the calorimetric procedure